

DECLARATION FOR PATENT APPLICATION

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled Recombinant antigen from the NS3 region of the hepatitis C virus
the specification of which

() is attached hereto.

(x) was filed on 07. August 1995 as Application Serial No. 08/511,759
and was amended on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, 1.56(a).

Foreign Priority Applications

I hereby claim foreign priority benefits under Title 35, United States Code 119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

			<u>Priority Claimed</u>
<u>P 44 28 705.4</u>	<u>Germany</u>	<u>12. August 1994</u>	Yes (x) No ()
(Number)	(Country)	(Day/Month/Year Filed)	
_____	_____	_____	Yes () No ()
(Number)	(Country)	(Day/Month/Year Filed)	

U.S. Priority Applications

I hereby claim the benefit under Title 35, United States Code, Section 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of the application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, Section 112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, Section 1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

<u>(Applic. Serial No.)</u>	<u>(Filing Date)</u>	<u>(Status patented/pending/abandoned)</u>
_____	_____	_____
(Applic. Serial No.)	(Filing Date)	(Status patented/pending/abandoned)

Power of Attorney

I hereby appoint the following attorneys to prosecute this application and transact all business in the Patent and Trademark Office connected therewith: Peter F. Felfe, Reg. No. 20,297; John E. Lynch, Reg. No. 20,940; Alfred H. Hemingway, Jr., Reg. No. 26,736; Vincent M. Fazzari, Reg. No. 26,879; Frederick H. Rabin, Reg. No. 24,488; Hallie R. Levie, Reg. No. 31,116; Marius J. Jason, Reg. No. 27,805; Charles A. Blank, Reg. No. 17,419; Norman D. Hanson, Reg. No. 30,946; F. Brice Faller, Reg. No. 29,532; Andrew L. Tiajolloff, Reg. No. 31,575; and John P. Luther, Reg. No. 32,261; my attorneys with full power of substitution and revocation; and Walter G. Weissenberger, Reg. No. 17,344. Address all telephone calls to _____, (212) 688-9200. Address all correspondence to:

FELFE & LYNCH
805 Third Avenue
New York, New York 10022

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

(1) Dr. Christoph SEIDEL

Full Name/Sole or First Inventor

Signature

Date

Residence: Ammerstr. 39, D-82362 Weilheim, Germany

German
Citizenship

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(2) Dr. Ursula-Henrike WIENHUES

Full Name/Second Joint Inventor

Signature

Date

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Citizenship

Post Office Address: same as above

(3) Urban SCHMITT

Full Name/Third Joint Inventor

[Signature]
Signature

10-25-95
Date

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(4) Dr. Manfred MOTZ

Full Name/Fourth Joint Inventor

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(5) Dr. Michael WIEDMANN

Full Name/Fifth Joint Inventor

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Signature

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Date

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Post Office Address: same as above

(6) Dr. Barbara UPMEIER

Full Name/Sixth Joint Inventor

[Signature]
Signature

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Date

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German
Citizenship

Post Office Address: same as above

(7) Dr. Erwin SOUTSCHEK

Full Name/Seventh Joint Inventor

[Signature]
Signature

10-31-95
Date

Residence: Enzianweg 49, D-82335 Berg, Germany

German
Citizenship

Post Office Address: same as above

HUBR 1067 PFF/NDH

To the Honorable Commissioner of Patents and Trademarks: Please record the attached original documents or copy thereof.

1. Name of conveying party(ies):

DR. CHRISTOPH SEIDEL
DR. URSULA-HENRIKE WIENHUS
URBAN SCHMITT
DR. MANFRED MOTZ
DR. MICHAEL WIEDMANN
DR. BARBARA UPMEIER
DR. ERWIN SOUTSCHEK

Additional name(s) of conveying party(ies) attached? ☐ Yes ☒ No

2. Name and address of receiving party(ies)

Name: BOEHRINGER MANNHEIM GmbH

Internal Address: Sandhofer Str. 112 -132

D-68305 Mannheim

GERMANY

Street Address: _____

City: _____ State: _____ Zip: _____

3. Nature of conveyance:

☒ Assignment

☐ Merger

☐ Security Agreement

☐ Change of Name

☐ Other _____

Execution Date: OCTOBER 31, 1995

Additional name(s) & address(es) attached? ☐ Yes ☐ No

4. Application number(s) or patent number(s):

If this document is being filed together with a new application, the execution date of the application is: _____

A. Patent Application No. (s)

08/511,759

B. Patent No. (s)

Additional numbers attached? ☐ Yes ☒ No

5. Name and address of party to whom correspondence concerning document should be mailed:

Name: FELFE & LYNCH

Internal Address: c/o Norman D. Hanson, Esq.

Street Address: 805 Third Avenue

City: New York State: N.Y. Zip: 10022

6. Total number of applications and patents involved: ☐

7. Total fee (37 CFR 3.41) \$40.00

☒ Enclosed

☐ Authorized to be charged to deposit account

8. Deposit account number: _____

(Attach duplicate of this page if paying by dep. acct.)

DO NOT USE THIS SPACE

9. Statement and signature.

To the best of my knowledge and belief, the foregoing information is true and correct and any attached copy is a true copy of the original document.

Norman D. Hanson
Name of Person Signing


Signature

November 21, 1995
Date

Total number of pages including cover sheet, attachments, and document: ☒

Mail documents to be recorded with required cover sheet information to:
Commissioner of Patents & Trademarks, Box Assignments
Washington, D.C. 20231

ASSIGNMENT

WHEREAS the undersigned [hereinafter (collectively)
"ASSIGNOR"] have invented certain new and useful improvements in

(Title of Application) Recombinant antigen from the NS3 region of the hepatitis C virus

for which an application for United States Letters Patent was executed concurrently herewith unless otherwise indicated.

WHEREAS
(Name and address of Assignee) Boehringer Mannheim GmbH
Sandhofer Str. 112 - 132
D-68305 Mannheim, Germany

a German corporation (hereinafter "ASSIGNEE") is desirous of acquiring the entire right, title and interest in the same:

Now, therefore, in consideration of the sum of one dollar (\$1.00), the receipt whereof is hereby acknowledged, and other good and valuable consideration, the said ASSIGNOR hereby sells, assigns and transfers unto said ASSIGNEE, full and exclusive right to the said invention in the United States and the entire right, title and interest in and to any and all Letters Patent which may be granted therefor.

Said ASSIGNOR hereby authorizes and requests the Commissioner of Patents and Trademarks to issue said Letters Patent to said ASSIGNEE, as the assignee of the entire right, title, and interest in and to the same, for the sole use and for the use of its successors, legal representatives, and assigns, to the full end of the term for which said Letters Patent may be granted, as fully and entirely as the same would have been held by said ASSIGNOR had this assignment and sale not been made.

Witness, the hand and seal of the ASSIGNOR on the date(s) indicated.

Date(s)

Signature(s)

10-25-95Dr. Christoph SEIDEL10-26-95Dr. Ursula-Henrike WIENHUS10-25-95Urban SCHMITT10-31-95Dr. Manfred MOTZ10-24-95Dr. Michael WIEDMANN11-18-95Dr. Barbara UPMEIER10-24-95Dr. Erwin SOUTSCHEK

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Applicant : Christophe Seidel, et al.
Serial No. : 09/896,032
Filed : June 29, 2001
For : METHOD FOR DETERMINING EARLY HCV
SEROCONVERSION
Art Unit : 1648
Examiner : Donna C. Wortman

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION

Dr. Ursula-Henrike Wienhues-Thelen hereby states as follows:

1. I am one of the coinventors of the invention described in the above referenced patent application. At the time the original application in the series of applications leading to the present application was filed, I was known as Ursula-Henrike Wienhues. "Wienhues-Thelen" is my married name.
2. I am familiar with the prosecution of the above referenced application, and the applications filed and prosecuted before it.
3. I have considered the English language translation of JP06074956 provided by the Examiner, and I would like to comment on why it is irrelevant to the invention claimed in this application. For simplicity, I will refer to this document as "JP '956".
4. The JP '956 application discusses how HCV antibodies can be determined, in diluted sera when using a reducing buffer, using the NS3 antigen.
5. This is decidedly NOT the same thing as determining early seroconversion in a sample. The reasons for this are multifold.

6. First of all, antibodies that are present in an early seroconversion sample differ significantly from those antibodies that are present in a high titer sample taken from a chronically ill patient, which was the sample type used in JP '956 before dilution sensitivity determination were carried out. For example, seroconversion antibodies differ from antibodies present at an advanced stage of infection, in that they show lower affinity, because they are mainly of IgM class, and have different specificity.
7. ~~In addition, seroconversion antibodies differ from others in their specificity~~ against viral epitopes. The impact of reducing buffer conditions on the presentation of epitopes of NS3 recognized by early seroconversion antibodies, and the effect of reducing buffer conditions on the binding affinity of epitopes to early seroconversion antibodies are not suggested by JP '956.
8. There is scientific evidence of this. For example, see WO 99/15901 (Chiron), Ziegler, et al., Poster Presentation, Berlin 1999; WO 99/54735 (Innogenetics), Wolter, et al., *Clin. Lab*, 43:125-135 (1997); Hino, *Intervirology*, 37:77-86 (1994); Barrera, et al., *Vox Sang*, 68:15-18 (1995); and Heyermann, et al., *Clin. Lab*, 44:903-905 (1998). Copies of these will be provided upon request.
9. The additional references that are used by the Examiner do not change these failings. Beach et al. discusses the temporal relationships of HCV RNA and antibody responses when chimpanzees were inoculated, but does not deal with human studies. No conclusions can be reached on the determination of HCV seroconversion in humans. Beach et al. profess this, at page 234, second paragraph of Discussions, lines 7-9.
10. The Vallari reference discusses serological markers of posttransfusion hepatitis C viral infection. At page 555, the second paragraph of the Discussion, line 11, the core antigen, not the NS3 antigen, was cited as the antigen to which response was

most frequent. Nothing at all suggests that one could use reducing buffers, in assays for NS3 antigens, to determine early seroconversion.

11. I further declare that all statements made herein of my own knowledge are true, and that all statements made on information or belief are believed to be true; and further that these statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements and the like so made may jeopardize the validity of this declaration, the subject application, or any patent issued thereon.

16 Oct 2004

Date

Ursula-Henrike Weinhuys-Thelen

Ursula-Henrike Weinhuys-Thelen